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(71) Applicant *(for all designated States except US)*: RHONE-POULENC RORER LIMITED [GB/GB]; RPR House, 50 Kings Hill Avenue, Kings Hill, West Malling, Kent ME19 4AH (GB).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: BOURZAT, Jean-Dominique [FR/FR]; Rhône-Poulenc Rorer Recherche Developpement, Centre de Recherche de Vitry-Alfortville, 13, quai Jules Guesde, BP14, F-94403 Vitry Sur Seine Cedex (FR). COMMERCON, Alain [FR/FR]; Rhone-Poulenc Rorer Recherche Developpement, Centre de Recherche de Vitry-Alfortville, 13 quai Jules Guesde, BP14, F-94403 Vitry Sur Seine Cédex (FR). FILOCHE, Bruno, Jacques, Christophe [FR/FR]; Rhone-Poulenc Rorer Recherche Developpement, Centre de Recherche de Vitry-Alfortville, 13 quai Jules Guesde, BP14, F-94403 Vitry Sur Seine Cedex (FR). HARRIS, Neil, Victor [GB/GB]; Rhone-Poulenc Rorer Limited, Rainham Road South, Dagenham, Essex RM10 7XS (GB). McCARTHY, Clive [GB/GB]; Rhone-Poulenc Rorer Limited, Rainham Road South, Dagenham, Essex RM10 7XS (GB).

(74) Agent: LEE CAFFIN; Rhone-Poulenc Rorer Limited, Patent Department, Rainham Road South, Dagenham, Essex RM10 7xs (GB).

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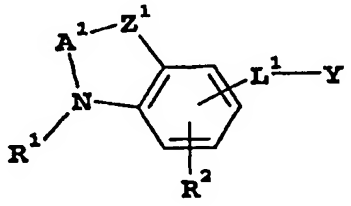
(54) Title: AZA-BICYCLES WHICH MODULATE THE INHIBITION OF CELL ADHESION



(I)

(57) Abstract

The invention is directed to physiologically active compounds of formula (I) wherein R^1 represents R^3–Z^3–, R^3–L^2–R^4–Z^3–, R^3–L^3–Ar^1–L^4–Z^3– or R^3–L^3–Ar^1–L^2–R^4–Z^3–; R^2 represents hydrogen, halogen, lower alkyl or lower alkoxy; A^1 represents a straight chain C_{1-3}alkylene linkage optionally substituted by one or more groups chosen from alkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, imino, oxo, thioxo, or alkyl substituted by –ZR^6, –NY^1Y^2, –CO_2R^6 or –C(=O)–NY^1Y^2; L^1 represents a direct bond; an alkenylene, alkylene, alkynylene, cycloalkenylene, cycloalkylene, heteroaryldiyl, heterocycloalkylene or arylene linkage each optionally substituted by (a) an acidic functional group, cyano, oxo, –$S(O)_mR^9$, R^3, –C(=O)–R^3, –C(=O)–OR^3, –$N(R^8)$–C(=O)–R^9, –$N(R^8)$–C(=O)–OR^9, –$N(R^8)$–SO_2–R^9, –NY^4Y^5 or –$[C(=O)–N(R^{10})–C(R^5)(R^{11})]_p$–C(=O)–$NY^4Y^5$, or by (b) alkyl substituted by an acidic functional group, or by $S(O)_mR^9$, –C(=O)–NY^4Y^5 or –NY^4Y^5; a –$[C(=O)–N(R^{10})–C(R^5)(R^{11})]_p$– linkage; a –$Z^2$–$R^{12}$– linkage; a –C(=O)–$CH_2$–C(=O)– linkage; a –$R^{12}$–$Z^2$–$R^{12}$– linkage; a –$C(R^4)(R^{13})–[C(=O)–N(R^{10})–C(R^5)(R^{11})]_p$– linkage; or a –$L^5$–$L^6$–$L^7$– linkage; Z^1 is $C(R^7)(R^{7a})$, C(=O) or CH(OH); Y is carboxy or an acid bioisostere; and the corresponding N-oxides, and their prodrugs; and pharmaceutically acceptable salts and solvates of such compounds and their N-oxides and prodrugs. Such compounds have valuable pharmaceutical properties, in particular the ability to regulate the interaction of VCAM-1 and fibronectin with the integrin VLA-4 ($\alpha 4\beta 1$).